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10/080,101	02/19/2002	Klaus Gregorius Nielsen	674542-2003	7906

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FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/080,101	NIELSEN ET AL.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6 and 8-38* is/are pending in the application.

4a) Of the above claim(s) *9,13 and 26-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6, 8, 10-12, and 14-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,4-6 and 8-38* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647, Examiner Jon Lockard.

2. The Amendment filed 24 May 2005 has been received and entered in full. Claims 14 and 15 have been amended and claims 26-38 are withdrawn from consideration as being drawn to a non-elected invention. The claims also read upon the following species: Dextran as the polyhydroxypolymer. Accordingly, claims 9 and 13 have been withdrawn from further consideration as being drawn to a non-elected invention as they either do not read on the elected invention (i.e., Dextran) or the recited properties of the elected invention (i.e., water soluble). Therefore, claims 1, 4-6, and 8-38 are pending and claims 1, 4-6, 8, 10-12, and 14-25 are the subject of this Office Action.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

4. The Information Disclosure Statement (IDS) submitted on 30 November 2004 has been considered by the Examiner.

Withdrawn Objections and/or Rejections

5. The objection to claim 15 as set forth on page 3 (¶ 7) in the previous Office Action (mailed 24 November 2004) is withdrawn in view of Applicants' amendments (filed 24 May 2005).

6. The rejection of claim 14 under 35 U.S.C. §112(2), as set forth at page 3 (¶ 8) in the previous Office Action (mailed 24 November 2004) is withdrawn in view of Applicants' amendment of said claim which now recites units for the weight (filed 24 May 2005).

7. The rejection of claims 1, 4-6, 8-14, and 16-24 under 35 U.S.C. §102(b) as being anticipated by Cheronis et al. (U.S. Pat. No. 5,573,916), as set forth at pages 3-4 (¶ 9-10) in the previous Office Action (mailed 24 November 2004) is withdrawn in view of Applicants' arguments (filed 24 May 2005).

8. The rejection of claims 1, 4-6, 8-10, 13, and 16-25 under 35 U.S.C. §102(b) as being anticipated by Chisari et al. (U.S. Pat. No. 5,709,995), as set forth at page 4 (¶ 12-13) in the previous Office Action (mailed 24 November 2004) is withdrawn in view of Applicants' arguments (filed 24 May 2005).

9. The rejection of claims 1, 4-6, 8-11, 13, and 16-25 under 35 U.S.C. §102(b) as being anticipated by Chisari (U.S. Pat. No. 5,780,036), as set forth at page 5 (¶ 15-16) in the previous Office Action (mailed 24 November 2004) is withdrawn in view of Applicants' arguments (filed 24 May 2005).

New Objections and/or Rejections

Claim Objections

10. Claim 10 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 10 recites "wherein the polyhydroxypolymer is selected from naturally occurring polyhydroxy compounds and synthetic polyhydroxy compounds. Since these forms of polyhydroxy compounds represent all possible forms of polyhydroxy compounds, these limitations do not further limit claim 1 from which it depends. It is suggested that Applicant separate the claim into two separate claims, e.g.,:

> The immunogen according to claim 1, wherein the polyhydroxypolymer is a naturally occurring polyhydroxy compound.

> The immunogen according to claim 1, wherein the polyhydroxypolymer is a synthetic polyhydroxy compound.

11. Claim 11 is objected to for encompassing a non-elected inventions, e.g., acetan, amylopectin, etc...

Appropriate correction is suggested.

Claim Rejections - 35 USC § 112, 2nd Paragraph

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 4-5 and 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it recites "an amide bond or a peptide bond". Since a peptide bond refers to an amide linkage, it is not clear if the "peptide bond" recited in the claim refers to an amide bond or a bond different than an amide bond.

15. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it is unclear what is meant by the term "binds strongly". Since neither the art nor the specification provide an unambiguous definition of the term "binds strongly", the metes and bounds of the claim cannot be determined.

16. Claims 5 and 23 is rejected for depending from an indefinite claim.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole

would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 1, 4-6, 8, 10-12, and 14-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheronis et al. (U.S. Pat. No. 5,573,916) in view of Gregorius et al. (Hydrocoating: a new method for coupling biomolecules to solid phases. Journal of Immunological Methods. 181:65-73, 1995; cited by Applicants).

20. As set forth at pages 3-4 of the previous Office Action (mailed 24 November 2004), Cheronis et al. teaches an immunogenic construct comprising a carrier conjugated to a B-cell epitope and a helper T-cell epitope, wherein the epitopes can be from the same species or from different species (relevant to claims 1 and 20-23). Cheronis et al. also teach that the B-cell and T-cell epitopes can elicit antigen-presenting cells (relevant to claims 18-19). Cheronis et al. also teach that the carrier may be naturally-occuring, semisynthetic, or synthetic and may be dextran (including those with a molecular weight of 500,000 Da), cellulose, agarose, and polyacrylamide (See columns 5-6) (relevant to claims 1, 4-6, 8, 11-12, and 14). Cheronis et al. also teach that said immunogenic construct may contain epitopes (i.e., "peptides" or "constructs") from

bacteria, fungi, viruses, drugs, and chemicals (See column 3) (relevant to claims 16-17). Lastly, Cheronis et al. also teach that said immunogenic construct can be included in a pharmaceutical composition comprising a carrier (vehicle), water, (a diluent), or an adjuvant (See column 5) (relevant to claim 24.

21. However, Cheronis et al. does not teach or suggest that the epitopes or antigenic determinants are coupled to the carrier (e.g., dextran) via nitrogen atoms at their respective N-termini.

22. However, such teachings were known in the art at the time of the invention, as Applicants note in the instant specification (See page 4, lines 25-28). For example, Gregorius et al. teach the coupling of a biomolecule via nitrogen atoms at their respective N-termini (i.e., a peptide bond) to a tresyl-activated polyhydroxypolymer (water-soluble dextran) carrier substantially free of amino acid residues (See Figure 1 and page 67, left column) which, in the absence of evidence to the contrary, would be cleavable by a peptididase. It would have been obvious to a person of ordinary skill in the art to modify the teachings of Cheronis et al. to activate the water-soluble dextran with tresyl and directly couple the epitopes of Cheronis et al. (i.e., biomolecules) to the dextran as taught by Gregorius et al. One skilled in the art would be motivated to do so since the direct coupling of the epitopes to the carrier would not require the additional step of modifying the epitope by the addition of a cysteine and thus simplifying the preparation and not altering the nature of the epitope being coupled. The expectation of success is high since Gregorius et al. teach that the tresyl-activated water-soluble dextran readily binds peptides which possess nucleophilic groups, such as an amino group (See Figure 1 and page 66, right column).

23. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

24. Claims 1, 4-6, 8, 10-12, and 14-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chisari et al. (U.S. Pat. No. 5,709,995) in view of Gregorius et al. (Hydrocoating: a new method for coupling biomolecules to solid phases. Journal of Immunological Methods. 181:65-73, 1995; cited by Applicants).

25. As set forth at page 4 of the previous Office Action (mailed 24 November 2004), Chisari et al. teaches an immunogenic composition comprising a CTL epitope and a Helper T-cell epitope conjugated via the N-terminus to a carrier molecule, which includes but is not limited to, an immunogenic lipid, propylene glycol, polyethylene glycol, and other peptides (See columns 6, 10, 16, and 53-54) (relevant to claims 1, 4-6, 8, 10, 13, and 16-25. Chisari et al. also teach the above-mentioned immunogenic composition also comprising a pharmaceutically acceptable carrier, excipient, diluent, and/or adjuvant. Chisari et al. also teach that the pharmaceutical adjuvants include but are not limited to oil formulations, aluminum phosphate, aluminum hydroxide (See columns 14-17) (relevant to claims 24-25.

26. However, Chisari et al. does not teach or suggest that the epitopes or antigenic determinants are coupled to a dextran carrier via nitrogen atoms at their respective N-termini.

27. However, such teachings were known in the art at the time of the invention, as Applicants note in the instant specification (See page 4, lines 25-28). For example, Gregorius et al. teach the coupling of a biomolecule via nitrogen atoms at their respective N-termini (i.e., a peptide bond) to a tresyl-activated polyhydroxypolymer (water-soluble dextran) carrier substantially free

of amino acid residues (See Figure 1 and page 67, left column) which, in the absence of evidence to the contrary, would be cleavable by a peptididase. It would have been obvious to a person of ordinary skill in the art to modify the teachings of Chisari et al. to use tresyl-activated water-soluble dextran and directly couple the epitopes of Chisari et al. (i.e., biomolecules) to the dextran as taught by Gregorius et al. One skilled in the art would be motivated to do so since the direct coupling of the epitopes to the tresyl-activated carrier would not require the additional step of modifying the epitope by the addition of a cysteine and thus simplifying the preparation and not altering the epitope being coupled. The expectation of success is high since Gregorius et al. teach that the tresyl-activated water-soluble dextran readily binds peptides which possess nucleophilic groups, such as an amino group (See Figure 1 and page 66, right column).

28. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

29. Claims 1, 4-6, 8, 10-12, and 14-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chisari (U.S. Pat. No. 5,780,036) in view of Gregorius et al. (Hydrocoating: a new method for coupling biomolecules to solid phases. Journal of Immunological Methods. 181:65-73, 1995; cited by Applicants).

30. As set forth at page 5 of the previous Office Action (mailed 24 November 2004), Chisari teaches an immunogenic composition comprising a CTL epitope and a Helper T-cell epitope conjugated via the N-terminus to a carrier molecule, which includes but is not limited to, an immunogenic lipid, cellulose, and other peptides (See columns 2-3, 5-6, 10-11, and 14) (relevant to claims 1, 4-6, 8, 10-11, and 16-25). Chisari also teaches the above-mentioned immunogenic

composition also comprising a pharmaceutically acceptable carrier, excipient, diluent, and/or adjuvant. Lastly, Chisari also teaches that the pharmaceutical adjuvants include but are not limited to aluminum hydroxide (See columns 3 and 13-15) (relevant to claims 24-25).

31. However, Chisari does not teach or suggest that the epitopes or antigenic determinants are coupled to a dextran carrier via nitrogen atoms at their respective N-termini.

32. However, such teachings were known in the art at the time of the invention, as Applicants note in the instant specification (See page 4, lines 25-28). For example, Gregorius et al. teach the coupling of a biomolecule via nitrogen atoms at their respective N-termini (i.e., a peptide bond) to a tresyl-activated polyhydroxypolymer (water-soluble dextran) carrier substantially free of amino acid residues (See Figure 1 and page 67, left column) which, in the absence of evidence to the contrary, would be cleavable by a peptididase. It would have been obvious to a person of ordinary skill in the art to modify the teachings of Chisari to use tresyl-activated water-soluble dextran as the carrier and directly couple the epitopes of Chisari (i.e., biomolecules) to the dextran as taught by Gregorius et al. One skilled in the art would be motivated to do so since the direct coupling of the epitopes to the tresyl-activated carrier would not require the additional step of modifying the epitope by the addition of a cysteine and thus simplifying the preparation and not altering the nature of the epitope being coupled. The expectation of success is high since Gregorius et al. teach that the tresyl-activated water-soluble dextran readily binds peptides which possess nucleophilic groups, such as an amino group (See Figure 1 and page 66, right column).

33. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Summary

34. No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JML
September 12, 2005

ROBERT S. LANDSMAN, PH.D.
PRIMARY EXAMINER